Inhibitors of Memapsin 2 and Use Thereof ld Koelsch, Jordan J. N. Tang, Lin Hong, and Arun K of U.S.S.N. 09/603,713

April 27, 2001 Atty. Docket No.: OMRF 182 DIV

FIG.

NILVDTGSSN DSGTTNLRLP GELGTDLVSI RPDDSLEPFF GIDHSLYTGS NIFPVISLYL STGTVMGAVI DMEDCGYNIP QHDDFADDIS SFVEMVDNLR GKSGQGYYVE MTVGSPPQTL STYRDLRKGV YVPYTQGKWE ILGLAYAEIA NLFSLQLCGA GFPLNQSEVL ASVGGSMIIG INGQDLKMDC KEYNYDKSIV PDGFWLGEQL VCWQAGTTPW PVEDVATSQD DCYKFAISQS QWRCLRCLRQ ACHVHDEFRT AAVEGPFVTL FFINGSNWEG FMLPLCLMVC LHRYYQRQLS ITILPQQYLR YYEVIIVRVE ARKRIGFAVS NIAAITESDK IKAASSTEKF AYVMAAICAL PHGPNVTVRA DSLVKQTHVP FAVGAAPHPF EEPEEPGRRG MEGFYVVFDR LWYTPIRREW KKVFEAAVKS MGEVTNQSFR QTDESTILMTI LLK* 36p 438 188 238 138 288 338 388 38 & &

QTDEST GFAVSA The →Promemapsin 2-T2 → Promemapsin 2-T1 MASMTGGQQMGRGSMAGVL MASMTGGQQMGRGSMAGVL

DYBYSKE DYBOLL

LGLRLPRETD

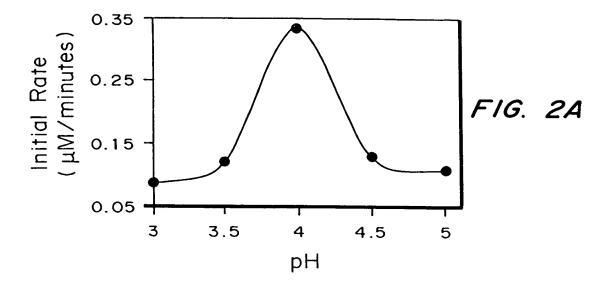
PLRSGLGGAP

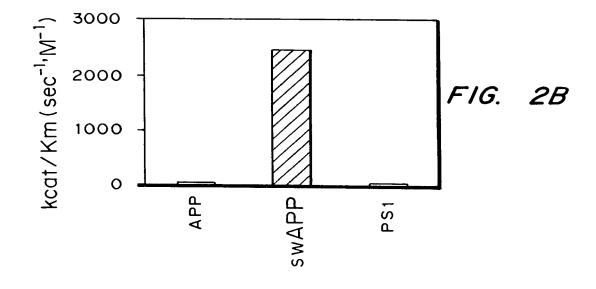
AHGTQHGIRL

1v MASMTGGQQM GRGSMAGVLP

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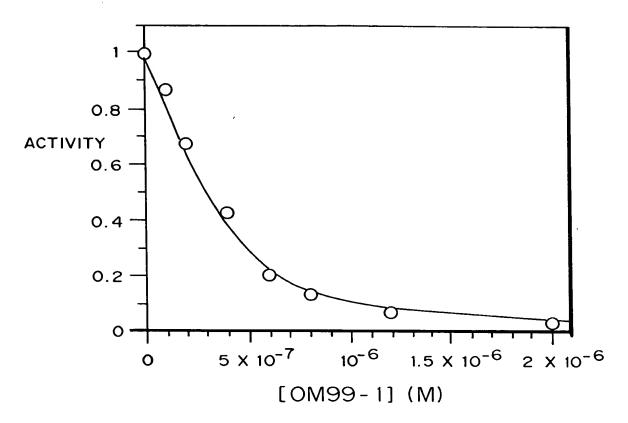
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FIG. 4A



[Mep2] = $0.47 \mu M$

[Fluo. Substrate] = $29.9 \mu M$

Buffer: Na Acetate O.1 M, 5% DMSO, pH 4.5 at 37°C

Excitation at 350 nm Emission at 490 nm

Parameter	Value	Std. Error
Ki	6.84 e - 8	2.72 e - 9

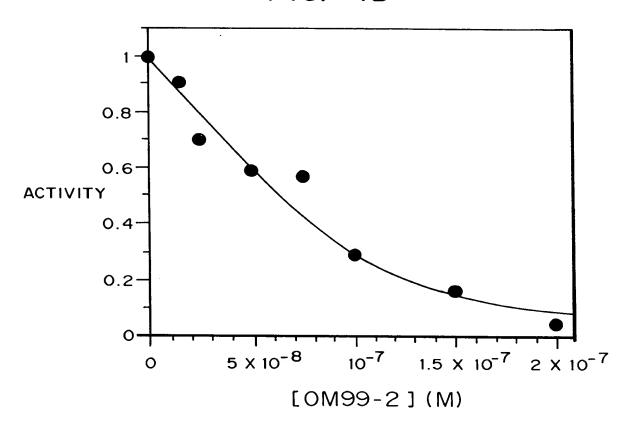
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FIG. 4B

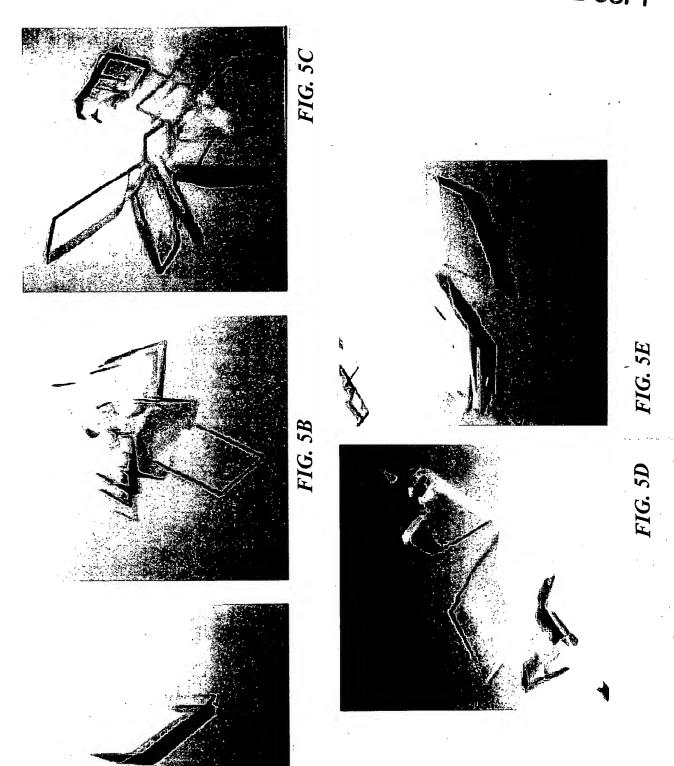


[E] $o = 0.11 \mu M$ [Fluo Substrate] = $29.9 \mu M$

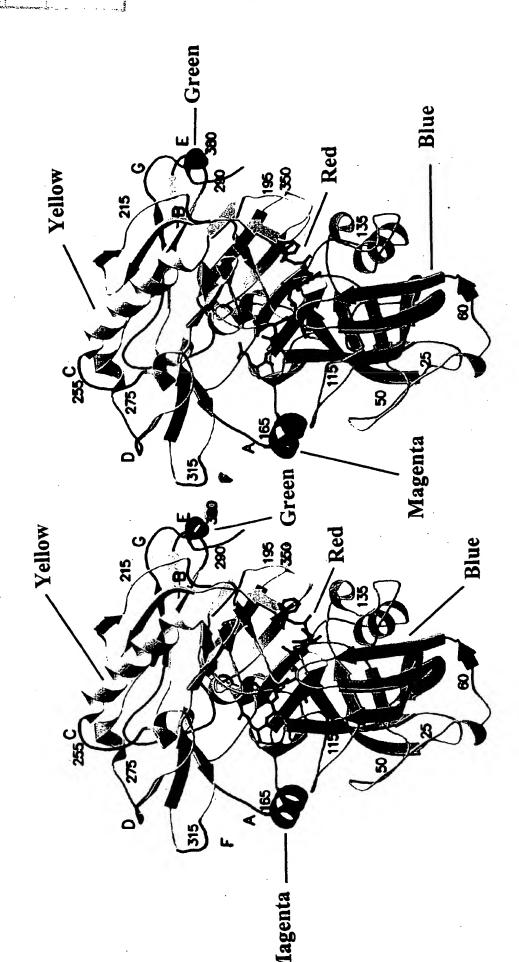
Parameter	Value	Std. Error
Ki	9.58e-9	2.86e - 10

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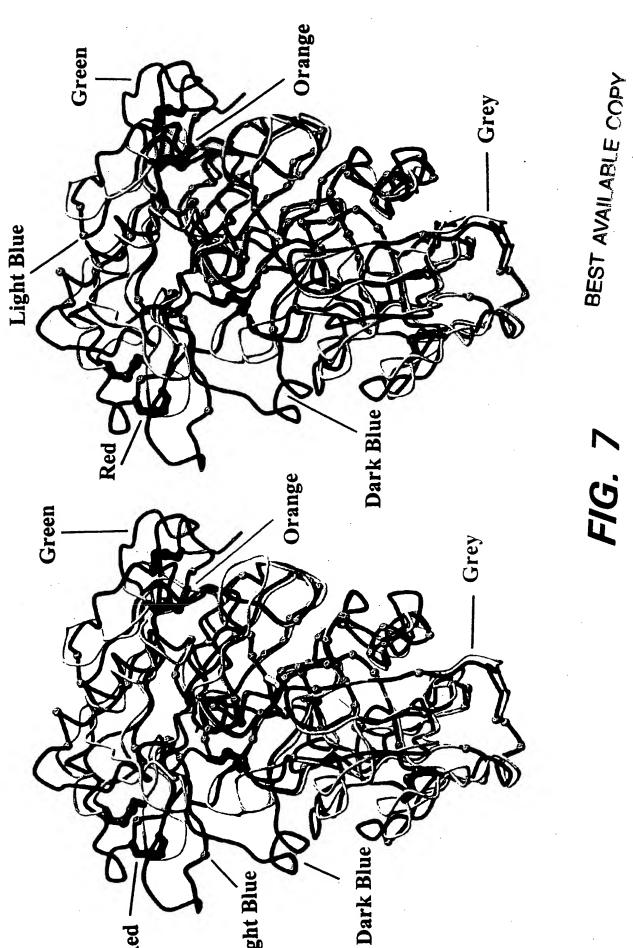
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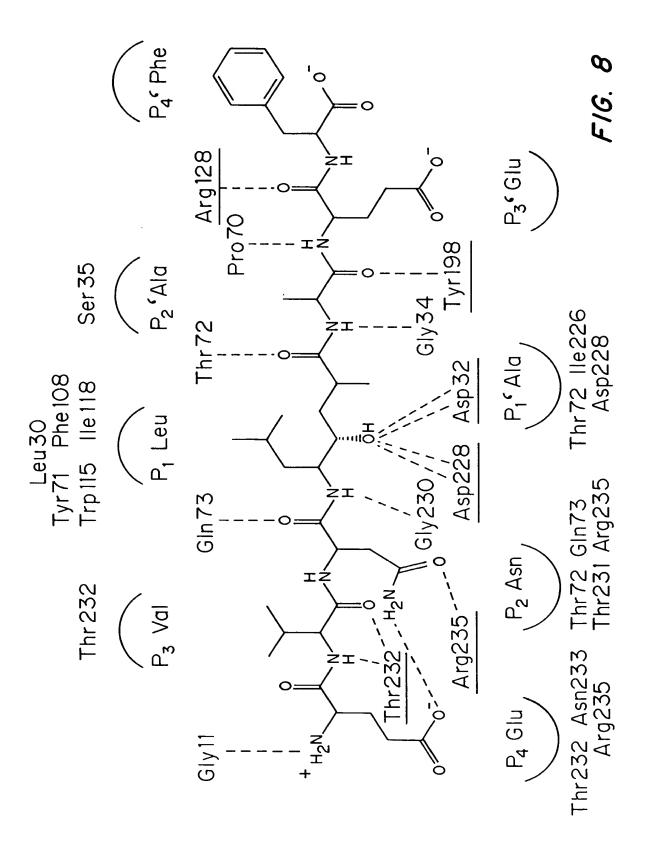


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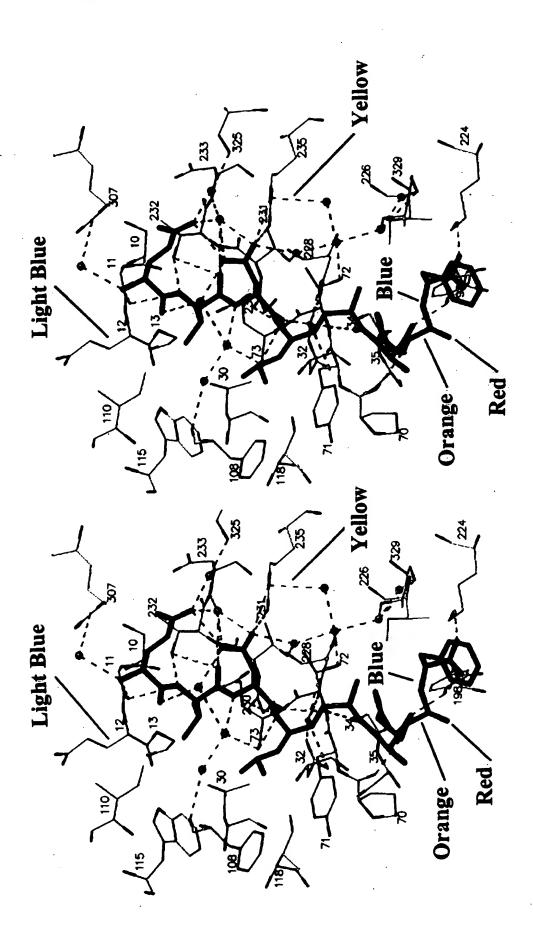


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. Ghosh

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P₁ Leu

$$P_3$$
 Val A^{--B} P_2 P_1

FIG. 10

 P_4 Glu

$$P_2$$
 Asn
$$P_2$$
 Asn
$$P_3$$

$$P_4$$

$$P_4$$

$$P_4$$

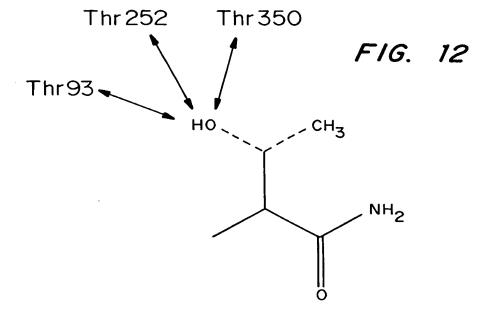
$$P_4$$

$$P_5$$

FIG. 11

DOGATUMS DAROCH

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P₁ Leu